Remarks/Arguments

Claims 1-25 are pending in this application and stand rejected on various grounds. An earlier rejection under 35 U.S.C. 112, first paragraph for alleged lack of enablement has been withdrawn in view of applicants' arguments. The rejections under 35 U.S.C. 112, first paragraph for alleged lack of adequate written description, and under 35 U.S.C. 102(a) have been maintained from the earlier Office Actions.

Both rejections are respectfully traversed.

Claim Rejections - 35 U.S.C. § 102

Claims 1-5, 9-11, 14-19, and 22 have been rejected under 35 USC 102(a) as allegedly being anticipated by Leung et al., Abstract, 1998.

As discussed in Applicants' previous response, the law clearly establishes that an inventor's own work may not be prior art under 35 U.S.C. §102(a) even if it has been disclosed to the public in the manner or form which would otherwise fall under §102(a). The cited Abstract is co-authored by (1) Woon-Lam S. Leung, (2) James R. Schwarz, and (3) John C. Joly. Co-authors (1) and (2) are named inventors in the present application. Enclosed are Declarations signed by these two inventors confirming that the work relating to the recovery of refractile particles containing a heterologous polypeptide, such as IGF-I, from bacterial periplasm, as claimed in the present application, is the joint invention of Woon-Lam S. Leung and James R. Schwarz, to which John C. Joly made no inventive contribution.

In view of the attached Declarations, under In re Katz, 687 F.2d 450 (CCPA, 1982), the present rejection should be withdrawn.

Claim Rejections - 35 U.S.C. § 112, first Paragraph

Claims 1-25 remain rejected under 35 U.S.C. § 112, first paragraph for alleged lack of adequate written description for the claimed subject matter. According to the rejection, the "claims are genus claims encompassing any nucleic acid encoding any phage lysozyme of any structure and amino acid sequence. The scope of the claims includes many nucleic acids

encoding many phage lysozyme with widely differing structural, chemical, and physical characteristics." The Examiner adds that "the genus is highly variable because a significant number of structural differences between genus members is permitted." Finally, the Examiner states that "[n]either the specification nor the general knowledge of those skilled in the art provide evidence of any significant structural property and amino acid sequence which would be expected to be common to the members of the genus. Thus, the disclosed plasmid pIGFLysAra containing a nucleotide sequence encoding T4-lysozyme and ara promoter is not representative of the claimed genus since other members of the genus have different amino acid sequences and structures."

Applicants disagree and, again, vigorously traverse the rejection.

Compliance with the written description requirement should be examined for the invention claimed

It is axiomatic that compliance with the conditions of patentability, including the written description requirement set forth in 35 U.S.C. 112, first paragraph, must be examined for the claimed invention. In the present case, the claimed invention is a method for recovering refractile bodies from bacterial periplasm in which the polypeptide is insoluble. The claimed method is characterized by coordinated expression of nucleic acid encoding a polypeptide and nucleic acid encoding a phage lysozyme in bacterial cells. The phage lysozyme is under the control of a promoter with low basal expression or an inducible promoter, and the polypeptide is expressed under the control of an inducible promoter. By placing the expression of the nucleic acid encoding the heterologous polypeptide and the lysozyme, respectively, under the control of separate promoters, one can independently regulate their expression during fermentation. When expression of the nucleic acid encoding the phase lysozyme is induced after about 50% or more of the heterologous polypeptide has accumulated, and when the conditions are selected such that the heterologous polypeptide is secreted into the periplasm of the bacterial cell as an aggregate and the phage lysozyme accumulates in the cytoplasmic compartment (as required by the language of claim 1), release of the insoluble refractile particles containing the heterologous polypeptide from the entanglement with the peptidoglycan layer becomes highly efficient.

The novelty of this process resides in the method steps discussed above. A review of the specification should make it clear that the independent control of the nucleic acid molecules encoding the lysozyme and the heterologous polypeptide, respectively, and the timing of the two expression steps are essential for the function/operation of the claimed invention. In contrast, the identity of a particular nucleic acid, either encoding the lysozyme or the polypeptide, is not essential to the claimed invention. Accordingly, the variability of the genus must be examined with regard to the process steps. Since the process steps are well defined and leave little room for variability, one of skill in the art would recognize that applicants were in the possession of the invention within the full scope of the claims pending at the time of making the invention.

The Examiner's attention is respectfully directed to Example 28 of the Revised Interim Written Description Guidelines Training Materials, which is analogous to the present situation and demonstrates the proper analysis for this type of invention.

The present rejection should not stand, even if the identity of the lysozyme and the promoter controlling the lysozyme were a critical part of the invention

Even if one assumes arguendo that the identity of the lysozyme and the promoter which controls its expression are a critical part of the claimed invention, the present rejection should still be withdrawn, since a *prima facie* case of lack of written description has not been established.

The mere fact that a genus might be variable is not a sufficient reason for a finding that the written description, based on a limited number of embodiments, is not adequate. In addition to pointing to the variability of a genus, such as structural differences between the members of a genus, the Examiner must establish that such differences matter and make it likely that the operability of the claimed invention depends on the specific structure. Such showing has not been made in the present case. In fact, Example 1 demonstrates that in addition to the T4-lysozyme, the use of the exogenous HEW-lysozyme increased the recovery of IGF-I refractile particles relative to control (from 28-33% to 42-52%) (see, page 42, lines 9-11, and Table 3). While the improvement obtained with T4-lysozyme was better (>90%), both lysozymes produced improvement relative to the control. These two exemplified embodiments establish that various

species within the genus of lysozymes are suitable for practicing the invention, which, in turn, means that one skilled in the art would reasonably conclude that Applicants were in the possession of this aspect of the invention at the time of making the invention.

The position that the genus of the promoters controlling the expression of the lysozyme lacks sufficient written description has similarly no support either in the Examiner's arguments or in the general state of the art at the time the claimed invention was made. The sole function of the promoter controlling the expression of the lysozyme (a promoter with low basal expression or an inducible promoter) is to provide for a controlled expression of the lysozyme, which is independent from the expression of the heterologous protein. Promoters with low basal expression and inducible promoters were well known in the art at the time the present invention was made, and are discussed on pages 18-19 and 21-23 of the specification. In view of this, there is not reason (and the Examiner certainly did not provide one) that would make a skilled person conclude that Applicants were not in the possession of the genus of "promoters with low basal expression" or of the genus of "inducible promoters."

Finally, applicants note that the issuance of U.S. Patent Nos. 6,180,367 and 6,258,560 on a related invention, claiming the same priority date as the present application, without any limitation on the scope of "phage lysozymes" further supports Applicants' arguments in the present case. It is realized that each application is examined on its own merits, however, it is desirable that a consistent approach is used and similar conclusions are reached in closely related cases, where the disclosures are similar.

In view of the foregoing arguments, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

All claims pending in this application are believed to be in prima facie condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any additional fees for extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39766-0128A).

Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

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